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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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PILLSBURY WINTHROP SHAW PITTMAN LLP
P.O BOX 10500
McLean, VA 22102

EXAMINER	
REDDIG, PETER J	
ART UNIT	PAPER NUMBER
1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
31 DAYS	03/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,143	JENKINS, JOHN	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-33* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 1-18, drawn to a method of administering chemotherapy, comprising administering a first agent that attenuates Topo II activity and administering a second agent that inhibits HSP90 activity.

Group 2, claim(s) 19-21, drawn to a delivery system for use in a gene therapy technique, said delivery system comprising: (i) a first DNA molecule encoding for a protein which directly or indirectly attenuates Topoisomerase II activity; and (ii) a second DNA molecule encoding for a protein which directly or indirectly inhibits Heat Shock Protein 90 activity; wherein said DNA molecules are capable of being transcribed to allow the expression of said proteins and thereby be effective for chemotherapy.

Group 3, claim(s) 22, 24, 25, and 26, drawn to a method of screening a first and a second compound, to test whether or not said compounds has efficacy for use in combination as a chemotherapy, comprising: (a) exposing said compounds to Topoisomerase II and evaluating whether or not said compounds bind thereto; (b) exposing said compounds to Heatshock Protein 90 and evaluating whether or not said compounds bind thereto; and (c) selecting a first and second compound, wherein at least one compound binds to Topoisomerase II and at least one compound binds to Heatshock Protein 90 for use in combination as a chemotherapy.

Group 4, claim(s) 23, 31, 32, and 33, drawn to a method of screening compounds, to test whether or not said compounds have efficacy for use in chemotherapy, comprising: (a) exposing said compounds to Topoisomerase II and evaluating whether or not said compounds bind thereto; (b) exposing said compounds to Heatshock Protein 90 and evaluating whether or not said compounds bind thereto; and (c) selecting compounds that bind to Topoisomerase II and to Heatshock Protein 90 for use in chemotherapy.

Group 5, claim(s) 27, drawn to a method of screening a compound, to test whether or not said compound is carcinogenic, comprising exposing said compound to Topoisomerase II and

Heatshock Protein 90 to evaluate whether or not said compound promotes interaction between Topoisomerase II and Heatshock Protein 90.

Group 6, claim(s) 28, drawn to an in vitro method for diagnosing whether or not a subject has cancer, comprising: (i) detecting the level of activity of HSP90 and Topoisomerase II from a sample of cells from said subject; and (ii) comparing the level of activity of HSP90 and Topoisomerase II in said sample relative to activity of HSP90 and Topoisomerase II from a non-cancerous sample.

Group 7, claim(s) 28, drawn to an in vitro method for diagnosing whether or not a subject is likely to develop cancer, comprising: (i) detecting the level of activity of HSP90 and Topoisomerase II from a sample of cells from said subject; and (ii) comparing the level of activity of HSP90 and Topoisomerase II in said sample relative to activity of HSP90 and Topoisomerase II from a non-cancerous sample.

Group 8, claim(s) 28, drawn to an in vitro method for diagnosing whether or not a subject has cancer, comprising: (i) detecting the expression levels of HSP90 and Topoisomerase II from a sample of cells from said subject; and (ii) comparing the expression levels of HSP90 and Topoisomerase II in said sample relative to expression levels of HSP90 and Topoisomerase II from a non-cancerous sample.

Group 9, claim(s) 28, drawn to an in vitro method for diagnosing whether or not a subject is likely to develop cancer, comprising: (i) detecting the expression levels of HSP90 and Topoisomerase II from a sample of cells from said subject; and (ii) comparing the expression levels of HSP90 and Topoisomerase II in said sample relative to expression levels of HSP90 and Topoisomerase II from a non-cancerous sample.

Group 10, claim(s) 29, drawn to an in vitro method for evaluating the suitability of chemotherapeutic treatment for administration to a subject, comprising: (i) detecting the level of activity of HSP90 and Topoisomerase II from a sample of cells from said subject; and (ii) comparing the level of activity of HSP90 and Topoisomerase II in said sample relative to activity levels of HSP90 and Topoisomerase II from a non-cancerous sample.

Group 11, claim(s) 29, drawn to an in vitro method for evaluating the suitability of chemotherapeutic treatment for administration to a subject, comprising: (i) detecting expression levels of HSP90 and Topoisomerase II from a sample of cells from said subject; and (ii) comparing the expression levels of HSP90 and Topoisomerase II in said sample relative to expression levels of HSP90 and Topoisomerase II from a non-cancerous sample.

Group 12, claim(s) 30, drawn to an in vitro method for monitoring the effectiveness of a chemotherapy for treating a subject, comprising: (i) detecting the level of activity of HSP90 and Topoisomerase II from a sample of cells from said subject; and (ii) comparing the level of activity of HSP90 and Topoisomerase II in said sample relative to activity expression levels of HSP90 and Topoisomerase II from a non-cancerous sample.

Group 13, claim(s) 30, drawn to an in vitro method for monitoring the effectiveness of a chemotherapy for treating a subject, comprising: (i) detecting the expression levels of HSP90 and Topoisomerase II from a sample of cells from said subject; and (ii) comparing the expression levels of HSP90 and Topoisomerase II in said sample relative to expression levels of HSP90 and Topoisomerase II from a non-cancerous sample.

A national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. Unity of invention is fulfilled only when there is a technical relationship among the inventions involving one or more of the same or corresponding special technical features which define a contribution over the prior art. If there is no special technical feature, if multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims, see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(d).

The technical feature linking Groups 1-13 appears to be modulation of both Topo II activity and HSP 90 activity, a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. Unity of invention is fulfilled only when there is a technical relationship among the inventions involving one or more of the same or corresponding special technical features which define a contribution over the prior art. If there is no special technical feature, if multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims, see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(d).

The inventions listed as Groups 1-13 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature linking Groups 1-13 appears to modulation of both Topo II activity and HSP 90 activity.

However, Münster et al. (Clinical Cancer Res. 2001, 7:2228-2236, IDS) teaches synergistic induction of apoptosis when using the HSP-90 inhibitor 17-AAG and the Topo II inhibitor doxorubicin, an anthracenedione derivative, see Abstract, p.2233-left col. and Figure 6.

Therefore, the technical feature linking the inventions of Groups 1-13 does not constitute a special technical feature as defined by PCT Rule 13.2 as it does not define a contribution over the prior art.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Species Elections for Group 1

A. Claim 1 is generic to the following disclosed patentably distinct species of first agent that attenuates Topo II activity:

1. a Podophyllotoxin and derivatives and analogues thereof

2. an Anthracenedione and derivatives and analogues thereof

3. m-AMSA (amsacrine) and derivatives and analogues thereof

4. a Bisdioxopiperazine and derivatives and analogues thereof

5. a thiobarbiturate

6. Genistein and derivatives or analogues thereof

7. Pyrazoloacridine and derivatives or analogues thereof

8. compounds that bind to Topo II and inhibit its activity

9. compounds which prevent the transcription of Topo II

10. compounds which prevent the translation of Topo II

11. compounds which prevent the expression of Topo II

12. compounds which inhibit release of Topo II from intracellular stores,

13. compounds which increase the rate of degradation of Topo II

14. etoposide (VP16)

15. teniposide

16. Anthrracenedione Mitoxantrone

17. ICRF-154

18. ICRF-159

19. ICRF-187

20. ICRF-193

21. Merbarone or derivatives/analogues thereof

B. Claim 1 is generic to the following disclosed patentably distinct species of second agent that inhibits HSP90 activity:

1. compounds that bind to HSP90 and inhibit its activity

2. compounds which prevent the transcription of HSP90

3. compounds which prevent the translation of HSP90

4. compounds which prevent the expression of HSP90

5. compounds which inhibit release of HSP90 from intracellular stores

6. compounds which increase the rate of degradation of HSP90

7. Geldanamycin or a derivative or analogue thereof

8. 17-Allylamino, 17-demethoxygeldanamycin (17AAG)

9. Radicicol or a derivative or analogue thereof

C. Claim 1 is generic to the following disclosed patentably distinct species of what the chemotherapy is for:

1. cancer treatment

2. antibacterial treatments

3. antifungal treatments

5. the treatment of AIDS/HIV

6. the treatment of multiple sclerosis

7. the killing and inhibition of proliferation of any organism

8. prophylactic treatment

If Applicant elects group C-1 (cancer treatment), then Applicant must elect from species group D.

D. Claim 1 is generic to the following disclosed patentably distinct species of cancer:

1. solid tumors

2. bowel cancer

3. small lung cancer

4. non-small cell lung cancer

5. breast cancer

6. bladder cancer

7. malignant melanoma

8. paediatric tumours

If Applicant elects group D-8 (paediatric tumours), then Applicant must elect from species group E.

E. Claim 1 is generic to the following disclosed patentably distinct species of paediatric tumor:

1. neuroblastoma

2. leukaemias and lymphomas

If Applicant elects group A-14 (etoposide) AND C-1 (cancer treatment), then Applicant must elect from species group F.

F. Claim 1 is generic to the disclosed patentably distinct species of 35 cancers listed in claim 16. Applicant must elect ONE cancer from claim 16 for examination.

Claims 1-18 will be examined as drawn to the elected species.

Species Elections for Group 2

A. Claim 19 is generic to the 52 disclosed patentably distinct species of "what the chemotherapy is for" listed in claim 21. Applicant must elect ONE species of the 52 species of "what the chemotherapy is for" listed in claim 21.

In accordance with the decisions in *In re Harnisch*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984), restriction of a Markush group is proper where the compounds within the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility. In addition, a Markush group may encompass a plurality of independent and distinct inventions where two or more members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the other member(s) obvious under 35 USC 103. Since the decisions in *In re Weber*, 198 USPQ 328 (CCPA 1978) and *In re Hass*, 198 USPQ 334 (CCPA 1978), it is proper for the Office to refuse to examine that which applicants regard as their invention, if the subject matter in a claim lacks unity of invention, see MPEP 803.02.

The above species are independent or distinct because they comprise structurally distinct molecules and/or have different modes of operation and different effects. Further, each species would require different searches and the consideration of different patentability issues.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species from each species group above for the elected invention Group, even though this requirement is traversed. Applicant is advised that a reply to this requirement must include an identification of the species

that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103 of the other invention.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102,

103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Applicant is advised that the reply to this restriction requirement to be complete must include an election of the invention to be examined even though the requirement is traversed (37 CFR 1.143).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Peter J. Reddig, Ph.D.
Examiner
Art Unit 1642

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

PJR